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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,617	05/14/2001	Jerome B. Zeldis	9516-022	7262

20582 7590 03/20/2006

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,617	ZELDIS ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,61 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on February 28, 2003 is acknowledged. The requirement was made FINAL in the Office Action dated May 19, 2003.

Information Disclosure Statement

2. Applicant should note that simply citing a reference in applicant's arguments is not sufficient for Office consideration. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office. Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Applicant's Response Dated January 17, 2006

3. Claims 1-11 and 61-62 are pending. An action on the merits of claims 1-11 and 61-62 is contained herein below.

4. The rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Marx et al. Proc. Am. Soc. Clin. Onocology (1997), Vol. 18, page 454a (Marx); Pitot et al. Journal of Clinical Onocology (1997), Vol. 15, pages 2910-2919 (Pitot); and Priel et al. US 5,622,959 (Priel) in combination is maintained for the reasons of record set forth in the Office Action dated November 17, 2005.

Rejections of Record Set Forth in the Office Action Dated June 25, 2004

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx et al. Proc. Am. Soc. Clin. Onocology (1997), Vol. 18, page 454a (Marx); Pitot et al. Journal of Clinical Onocology (1997), Vol. 15, pages 2910-2919 (Pitot); and Priel et al. US 5,622,959 (Priel) in combination.

Applicant's arguments filed November 17, 2005 have been fully considered but they are not persuasive. Applicant contends that there is no motivation to combine the cited references, as *In re Kerkhoven* is not germane. Applicant further contends when thalidomide is co-administered with irinotecan to patients with metastic colorectal cancer, unexpected synergism occurs and a remarkable absence of gastrointestinal toxicity typically associated with irinotecan is observed. Applicant further argues that based on this showing, one of ordinary skill in the art would have reasonably extended the probative value of this result to other topoisomerase inhibitors and other types of cancers.

Contrary to applicant's assertions, the legal logic set forth in the instant rejection is very much germane. The precident set by *In re Kerkhoven* is not limited to applications/patents involving detergents as applicant asserts, and the precedent set is seen to be sufficient for establishing a prima facie case of obviousness. Furthermore, as set forth on page 4 of the Office Action dated April 20, 2005, as supported by *Ex. Parte Quadrantil*, 25 USPQ2d 1071 (Bd. Pat. Appl. & inter. 1992), the use of materials in combination, each of which is known to function for intended purpose, is prima facie

obvious. Applicant should note that *Ex. Parte Quadrantil* is drawn to the use of a combination of herbicides not detergents.

Applicant's argument that thalidomide was not an "approved" anti-cancer drug at the time of the invention is not germane. The disclosure of Marx is seen to pre-date applicant's earliest claim of priority and thus constitutes prior art as applied under recited statue. Furthermore, it is unclear what type of approval applicant is referring to. Applicant should note that FDA approval or approval from any other U.S. agency is not required under 35 U.S.C. 103. In fact, the prior art does not have to be published in the U.S. nor does the reference have to be in the English language.

In response to applicant's argument that the co-administration of thalidomide and irinotecan to patients with colorectal cancer unexpectedly showed an absence of gastrointestinal toxicity typically associated with irinotecan, it is noted that the features upon which applicant relies (i.e., co-administration of thalidomide and irinotecan to patients with colorectal cancer) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). If applicant wishes to use an argument of unexpected results for overcoming the instant rejection, applicant's showing should be commiserative with the scope of the claims. Arguing, "Those of ordinary skill in the art would have had no reason to believe that such synergism would not extend to the combination of thalidomide and other topoisomerase inhibitors...or types of cancer other than colorectal cancer" is not sufficient. If the results are "unexpected", how can the same results also be "expected"

to one of ordinary skill in the art? As applicant states, "unfavorable drug-drug interactions are well known to those skilled in the art, and such interactions are not often predictable."

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx et al. Proc. Am. Soc. Clin. Onocology (1997), Vol. 18, page 454a (Marx); Pitot et al. Journal of Clinical Onocology (1997), Vol. 15, pages 2910-2919 (Pitot); and Priel et al. US 5,622,959 (Priel) in combination.

Claims 61-62 are drawn to a method of treating primary cancer comprising administering a therapeutically elective amount of a topoisomerase inhibitor, or a pharmaceutically acceptable prodrug, salt, solvate, hydrate, or clathrate thereof, and a therapeutically effective amount of thalidomide, or a pharmaceutically acceptable salt or solvate thereof.

Marx teaches thalidomide as an antiangiogenic agent in the treatment of advanced cancer (1751). The cancers that are treated include brain, melanoma, breast, colon, mesothelioma and renal cell carcinoma. Thalidomide was administered as an oral daily dose of 100 to 500 mg/day.

Marx differs from the instantly claimed invention in that Marx does not teach the co-administration of a topoisomerase inhibitor. However, the deficiencies of Marx would have been obvious to one of ordinary skill in the art at the time of the invention when viewed in combination with the teachings of Pitot and Priel.

Pitot teaches the administration of CPT-11 [irinotecan] for the treatment of metastatic colorectal carcinoma. Pitot teaches that CPT-11 was administered in 500mL of 5% dextrose solution (page 2912, Treatment Administration).

Priel teaches that camptothecin (CPT) has a strong antitumor activity against a wide range of experimental tumors and human colon cancer (column 2, lines 39-45).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine thalidomide and a topoisomerase inhibitor for the treatment of colorectal cancer. As supported by *Ex parte Quadrantil*, 25 USPQ2d 1071 (Bd. Pat. Appl. & Inter. 1992), the use of materials in combination, each of which is known to function for intended purpose, is prima facie obvious. In the absence of some proof of a secondary nature or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, it would have been obvious to one of ordinary skill in this art at the time of the invention to co-administer two components (thalidomide and a topoisomerase inhibitor), each of which is recognized as having anti-cancer activity as applicant has done with the above cited references before them. Compounds with the functional limitation of topoisomerase inhibition and thalidomide are well recognized in the art for the treatment of cancer individually, and to combine these two classes of compounds to obtain the same result is indeed *prima facie* obvious.

Conclusion

10. Claims 1-11 and 61-62 are pending. Claims 1-11 and 61-62 are rejected. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

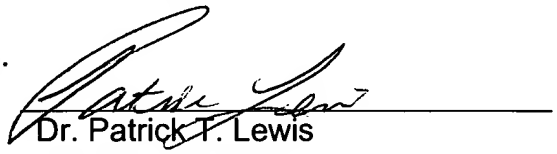
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Dr. Patrick T. Lewis
Primary Examiner
Art Unit 1623

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